REMARKS

Claims 1-4 and 6-23 are in the application. No claim is allowed. Claim 5 has been canceled. Claims 20-23 are newly presented. Claims 20-23 comprise the subject matter of canceled claim 5.

Claims 1-19 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Heidaran et al., U.S. Patent 6,309,670. This rejection is respectfully traversed. The Examiner recognizes that Heidaran et al. discloses compositions of collagen covalently cross-linked to an exogenous polysaccharide and a differentiation factor which may include BMPs and GDFs. However, the methods and compositions in Heidaran are directed to treatment of bone tumors. As defined by Heidaran, the treatment of bone tumors refers to minimizing or eliminating the presence of tumor cells at the site of administration, such as elimination of osteosarcoma in neuroectodermal tumors. See column 2, lines 47-50. The examples show, such as example 3, the anti-growth properties of the compositions. There is no suggestion that the factors induce or enhance chondrogenesis to produce cartilage. The target cells to which the compositions are exposed in Heidaran are tumor cells and the observation is that these cells are not enhanced or induced, but are rather inhibited. Therefore, the Examiner's characterization of Heidaran that it contemplates compositions and methods of exposing collagen-hyaluronic matrices comprising BMPs and GDFs to cells to induce or enhance chondrogenesis, is not accurate. Accordingly, it is submitted that Heidaran does not anticipate the present invention and withdrawal of the rejection is requested.

Claims 1-4 and 12-15 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Hattersley et al., U.S. Patent 5,902,785. This rejection is respectfully traversed. Hattersley does not disclose BMP-4 as a factor for inducing or enhancing chondrogenesis to produce cartilaginous tissue. Instead, in order to induce articular cartilage tissue formation and maintain that tissue, Hattersley requires the presence of at least two active substances, bone morphogenetic protein BMP-13, and a BMP which must be BMP-2, -4,-7 and/or -9. Applicant's claims however recite that it is sufficient to induce or enhance chondrogenesis solely with an effective amount of BMP-4 or a combination of BMP-4 and GDF-5, neither of which is taught in Hattersley. Hattersley does not even discuss GDF-5. There is no indication in Hattersley that

there is a recognition that BMP-4 alone can be used to induce or enhance chondrogenesis. The effective amount in Hattersley's compositions must contain BMP-13. Effective amounts of BMP-4 alone to induce or enhance chondrogenesis are not disclosed. It is therefore submitted that Hattersley does not anticipate the present claims and withdrawal of the rejection is requested.

Claims 1-19 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Adams et al., U.S. Patent 5,118,667. This rejection is respectfully traversed. Adams is directed to the stimulation of new bone formation by administering an effective dose of a bone growth factor such as BMP, and a pharmaceutically effective dose of an inhibitor of bone resorption, such as bisphosphate. There is no teaching of induction or enhancement of chondrogenesis to make cartilaginous tissue. Indeed, it is submitted that one of ordinary skill in the art would read Adams to suggest that only bone can be made using the invention disclosed therein.

The Examiner states that since the method discussed by Adams et al. contemplates administering compositions comprising bone growth factors in carrier matrices to regenerate bone tissue, the expected result would have been successful methods and compositions for the regeneration of cartilage. It is not known how the Examiner arrives at this conclusion from that premise. The production of bone is different from the production of cartilage-like materials. The distinction, for example, is noted by Hattersley in column 1, lines 19-44. Hattersley notes that although all of the BMPs appear to be involved in bone repair or bone maintenance, they only found that a certain BMP-12 related sub-family has tendon/ligament-like tissue inducing activity. Therefore, contrary to the Examiner's statement about Adams, it is submitted that one would not expect any particular BMP directed to repair or maintenance of bone to also have tendon/ligament-like tissue inducing activity. The art simply does not support this statement made by the Examiner characterizing Adams. It is therefore submitted that the present claims are unobvious over Adams and withdrawal of the rejection is respectfully requested.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be allowed. Enclosed is a check which includes excess claim fees in the amount of $344 and for the Petition for Extension of Time fee in the amount of $465. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

1. A method for inducing or enhancing chondrogenesis in cells comprising the step of exposing said cells to a matrix composition comprising [of] type I collagen and an effective amount of BMP-4 sufficient to induce or enhance chondrogenesis.
2. A method for inducing or enhancing chondrogenesis in cells comprising the step of exposing said cells to a matrix composition comprising [of] type II collagen and an effective amount of BMP-4 sufficient to induce or enhance chondrogenesis.
3. A method for inducing or enhancing chondrogenesis in cells comprising the step of exposing said cells to a matrix composition comprising [of] type I collagen, hyaluronate and an effective amount of BMP-4 sufficient to induce or enhance chondrogenesis.
4. A method for inducing or enhancing chondrogenesis in cells comprising the step of exposing said cells to a matrix composition comprising [of] type II collagen, hyaluronate and an effective amount of BMP-4 sufficient to induce or enhance chondrogenesis.
7. A method according to claim [5] 20, 21, 22 or 23 wherein said step of exposing said cells occurs *in vivo*.
9. A method according to claim [5] 20, 21, 22 or 23 wherein said step of exposing said cells occurs *in vitro*.